

- 3) To search for drugs as ligands or antagonists of the polypeptide encoded by the claimed polynucleotide;
- 4) To produce a variant or chimeric nucleotide or polypeptide;
- 5) In the creation of transgenic animals;
- 6) To detect polymorphisms in individuals;
- 7) For clinical therapy using the polypeptide or ligand.

The examiner further stated that the on page 6 that the disclosed polypeptide “has high homology to the N-methyl-D-aspartate receptor, as shown in Figure 2 of the instant Specification (Sucher, N.J., 1999, Accession No. T31068).” Further the examiner stated that the specification does not teach functional or structural characteristics of the amine receptor polypeptide recited in the claims.

Applicants respectfully disagree. First, the examiner may have mistaken the homology comparison because there is no N-methyl-D-aspartate receptor disclosed in the Figure 2. Further, support for the functional classification of the protein of SEQ ID NO:2 as being a member of aminergic receptor of GPCR can also be found in Figure 2. For example, the Blast alignment shows that SEQ ID NO:2 shares most of the functional domains with GPCR 58 which belongs to aminergic receptor family. In addition, Hmmer search results ([pfam.wustl.edu](http://pfam.wustl.edu)) on page 2 of Figure 2 shows that SEQ ID NO: 2 of the present invention has statistically significant homology to serotonin receptors and dopamine receptors in the aminergic receptor domains.

Examiner further stated, by citing a number of references (pages 6 -7), that the structurally similar protein could have different function, and one cannot rely upon structural similarity alone to determine the functionality of the protein.

Again, as recited above, the present invention is based more than one simple homology search. The determination of the function is involved in functional determination on the domain of the protein. For example, Hmmer search shows the protein of the present invention has serotonin receptors and dopamine receptors functional domains, so does the Prosite search, wherein the protein has GPCR signature domain (Figure 2). The utility of the receptor of the present invention is depicted on pages 4-9, Thus, this receptor would be a potential drug target for neurotransmitter related diseases.

Finally, the examiner addresses the references submitted to the Office and stated that the protein disclosed in the reference “is inconsistent with the peptide disclosed in the instant

specification as a rat NMDA receptor, as shown in Figure 2." However, Applicant would like to reiterate that the protein of the present invention is related to the aminergic (biogenic amines) receptor subfamily of the GPCR family (see page 2, first paragraph). The present invention is similar to GPCR 58 protein that belongs to aminergic family (see the previous response mailed on Oct. 9, 2002). The rat NMDA was not recited in the homology search of Figure 2. Thus, the rejection is moot.

Again, as stated in previously, the receptor of the present invention has substantially the same expression profile as disclosed in the reference by Borowsky et al., for example, the expression in stomach, kidney, as well as in brain. Moreover, the references are additional proof that the protein of the present invention functions as aminergic receptor.

In summary, supported by references submitted previously, the present invention meets the requirement of a specific, substantial and credible utility that is imposed by the Utility Guideline under 35 USC §101 and §112, 1<sup>st</sup> paragraph.

In view of the above remarks and amendments, Applicants respectfully submit that the application and claims are in condition for allowance, and request that the Examiner reconsider and withdraw the rejections. If for any reason the Examiner finds the application in condition for allowance, the Examiner is invited to call the undersigned to expedite prosecution of the application.

Respectfully submitted,

Date: May 16, 2003

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